EXHIBIT 106

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Mesothelioma: Risk Apportionment Among Asbestos Exposure Sources

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The mesothelioma epidemic in the United States, which peaked during the 2000–2004 period, can be traced to high-level asbestos exposures experienced by males in occupational settings prior to the full recognition of the disease-causing potential of asbestos and the establishment of enforceable asbestos exposure limits by the Occupational Safety and Health Administration (OSHA) in 1971. Many individuals diagnosed with mesothelioma where asbestos has been identified as a contributing cause of the disease have filed claims seeking compensation from asbestos settlement trusts or through the court system. An individual with mesothelioma typically has been exposed to asbestos in more than one setting and from more than one asbestos product. Apportioning risk for mesothelioma among contributing factors is an ongoing problem faced by occupational disease compensation boards, juries, parties responsible for paying damages, and currently by the U.S. Senate in its efforts to formulate a bill establishing an asbestos settlement trust. In this article we address the following question: If an individual with mesothelioma where asbestos has been identified as a contributing cause were to be compensated for his or her disease, how should that compensation be apportioned among those responsible for the asbestos exposures? For the purposes of apportionment, we assume that asbestos is the only cause of mesothelioma and that every asbestos exposure contributes, albeit differentially, to the risk. We use an extension of the mesothelioma risk model initially proposed in the early 1980s to quantify the contribution to risk of each exposure as a percentage of the total risk. The percentage for each specific discrete asbestos exposure depends on the start and end dates, the intensity, and the asbestos fiber type for the exposure. We provide justification for the use of the mesothelioma risk model for apportioning risk and discuss how to assess uncertainty associated with its application.

KEY WORDS: Asbestos; exposure; mesothelioma; risk apportionment; risk assessment

1. INTRODUCTION

The mesothelioma epidemic in the United States, which peaked during the 2000–2004 period,(1,2) is a result of high-level occupational exposure to asbestos that occurred prior to the full recognition of the disease-causing potential of asbestos and the establishment of enforceable asbestos exposure limits by the Occupational Safety and Health Administration (OSHA) in 1971. Workers, primarily men, were exposed in the mining and milling of raw asbestos, manufacture of asbestos-containing products, notably insulation and other construction materials, and the installation, maintenance, and repair of these materials. The time pattern of male mesothelioma incidence follows the pattern of asbestos consumption in the United States subject to a 30-year to 40-year lag, which reflects the latency period for this asbestos-associated disease (Fig. 1). Many individuals diagnosed with mesothelioma where asbestos has been

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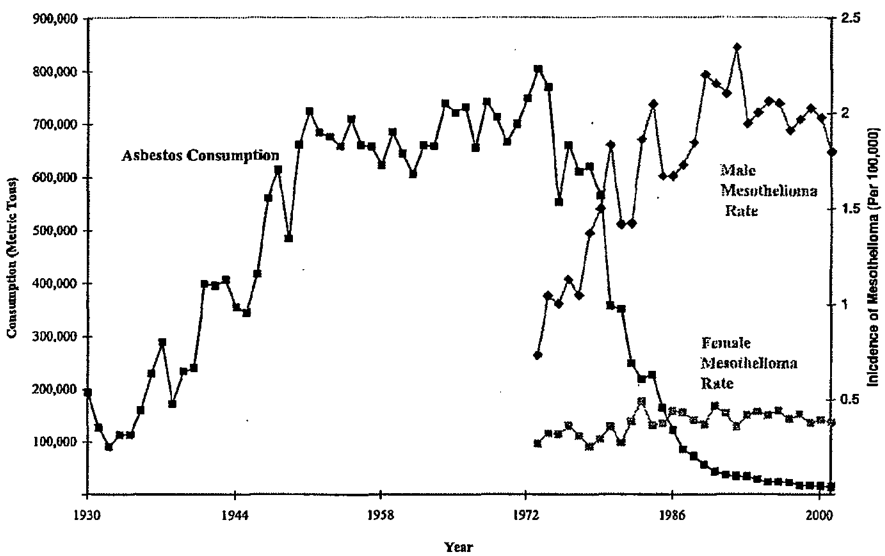

Fig. 1. Asbestos use in the United States and the mesothelioma rates for males and females.

identified as a contributing cause of the disease have filed claims seeking compensation from asbestos settlement trusts or through the court system. An individual with mesothelioma typically has been exposed to asbestos in more than one setting and from more than one asbestos product. The parties held responsible for asbestos exposure, such as manufacturers of asbestos-containing products or owners of the facilities where the exposures occurred, are expected to provide funds to satisfy the claims. In this article we address the following question: If an individual with mesothelioma where asbestos has been identified as a contributing cause were to be compensated for his or her disease, how should that compensation be apportioned among those responsible for the asbestos exposures?

A model for mesothelioma risk that depends on asbestos exposure intensity and time since first exposure (TSFE) was developed in the early 1980s. This model has been expanded and used by regulatory agencies, among others, in the United States and abroad for analyzing mesothelioma risk associated with asbestos exposure and developing risk management alternatives.[3–7] The expanded model may be used to calculate the risk, or equivalently the probability, of mesothelioma as a function of a profile of historical asbestos exposures. The model incorporates each specific discrete exposure of the profile as a distinct component contributing to risk. The sum of the risk components equals the total risk of mesothelioma due to asbestos exposure. The ratio of each risk component to the total risk, multiplied by 100, may be interpreted as the percentage of the total mesothelioma risk associated with the exposure for that component. Therefore, the set of all percentages defines an apportionment of risk among the specific asbestos exposure sources, which, in turn, may be used to assign shares of any monetary award among parties responsible for the exposures.

2. THE MODEL

Mesothelioma risk is the sum of the risks associated with asbestos exposures plus a spontaneous background risk that is independent of asbestos exposure. For the asbestos exposure component of risk, each specific asbestos exposure is characterized by the elapsed time since it first occurred, TSFE, the intensity of exposure, and the asbestos fiber type. Mesothelioma risk increases as a power of TSFE, is assumed to be linearly related to exposure intensity, and varies systematically with asbestos fiber type.

The mesothelioma risk model was derived from the multistage model for carcinogenesis, which describes the biological process of tumor growth in individuals that eventually leads to malignancy.[3,5,8]

The most general form of the asbestos component of the mesothelioma risk model is:[6,9]

$$I(T) = k \cdot \int_0^{T-10} K(x) \cdot f(x) \cdot (T - x - 10)^{k-1}\, dx, \quad (1)$$

where T is age, $f(x)$ is exposure intensity at age x measured in units of fibers per cubic centimeter of air (f/cc), $K(x)$ is a mesothelioma potency factor that is determined by the fiber type for asbestos exposure at age x, the integrand is an approximation to the hazard function based on the multistage model with k stages to malignancy, and $I(T)$ is mesothelioma incidence, which also may be interpreted as the risk or probability of mesothelioma. Note that $I(T)$ is a function of time since exposure occurred, which is measured using age.

If there are n specific discrete exposures at different constant intensities, the model becomes:

$$\begin{aligned} P_A(T) &= P_B(T) + P_S(T) = K_B \cdot f_B \cdot (T-10)^k \\ &\quad + \sum_1^n K_i \cdot f_i \cdot ([T - t_{Fi} - 10]^k \\ &\quad - [T - t_{Li} - 10]^k), \end{aligned} \quad (2)$$

where

$T =$ age;
$P_A(T) =$ risk of mesothelioma at age T resulting from asbestos exposure, which is the sum of risks associated with background exposure, $P_B(T)$, and specific identifiable exposure sources, $P_S(T)$;
$K_B =$ potency factor that is specific for the fiber type in background exposure, most likely chrysotile;
$f_B =$ average intensity (f/cc) for background exposure;
$K_i =$ potency factor that is specific for the fiber type in the ith discrete exposure, which could be chrysotile ($K_i = K_C$), amosite ($K_i = K_{Am}$), crocidolite ($K_i = K_{Cr}$), or mixtures of these fiber types;
$f_i =$ average intensity for the ith discrete exposure (f/cc);
$t_{Fi} =$ age at first exposure for the ith discrete exposure ($T - t_{Fi}$ is the elapsed time from first exposure for the ith discrete exposure);
$t_{Li} =$ age at last exposure for the ith discrete exposure ($t_{Li} - t_{Fi}$ is the duration, D_i, of the ith discrete exposure);
$k =$ a parameter of the model that reflects the time pattern for mesothelioma formation.
(The terms raised to the power k are set to zero if they are negative.)

The model for total risk of mesothelioma includes a component, $P_0(T)$, for the risk of spontaneous background mesothelioma. Based on the general characteristics of the age distribution of cancer,[10,11] we suggest that the spontaneous background component of mesothelioma risk can be modeled as a power of age:

$$P_0(T) = K_0 \cdot T_0^k. \quad (3)$$

Therefore,

$$\begin{aligned} P(T) &= P_0(T) + P_B(T) + P_S(T) \\ &= K_0 \cdot T_0^k + K_B \cdot f_B \cdot (T-10)^k \\ &\quad + \sum_1^n K_i \cdot f_i \cdot [(T - t_{Fi} - 10)^k \\ &\quad - (T - t_{Li} - 10)^k]. \end{aligned} \quad (4)$$

The full model (Equation (4)) could be used to analyze the mesothelioma risk contribution of asbestos exposures identified with responsible parties versus the risk contribution from background exposures or the spontaneous background risk that is independent of asbestos exposure. Although that analysis could be useful for placing bounds on the risk contribution of responsible parties, we have not addressed that issue. Instead, we focus on apportioning risk among specific identifiable asbestos exposure sources.

2.1. Mesothelioma Risk Estimation

Evaluating the risk of mesothelioma using $P_S(T)$ requires numerical values for the parameters, $\{K_i\}$, k, of the model, and values for the exposure variables, T, $\{f_i\}$, $\{t_{Fi}\}$, and $\{t_{Li}\}$. As described in the next section, the parameters are estimated from studies of occupational cohorts that worked with asbestos. The exposure variables, which are facts that define a particular individual's exposure profile, are described through an example.

2.2. Model Parameters

We consider exposures to three fiber types, chrysotile, amosite, crocidolite, and mixtures of these fiber types. The potency parameters for the three fiber types are denoted as K_C, K_{Am}, and K_{Cr}. The values

for these parameters have been estimated from data in epidemiology studies of occupational cohorts.[6,7,9,12] The Environmental Protection Agency (EPA) and OSHA, the government agencies in the United States that regulate asbestos exposure, currently use a single mesothelioma potency value for all fiber types, $K_M = 1 \times 10^{-8}$. This potency value is based on analyses of data completed before 1986. Since 1986, there has been broad scientific support for a potency gradient for fiber types, with chrysotile being the least potent fiber type and crocidolite the most potent. A recent analysis of data from historical occupational studies by Hodgson and Darnton[12] indicates a potency gradient of 1:100:500 for chrysotile, amosite, and crocidolite, respectively. Berman and Crump,[9] in research that was conducted as part of the ongoing EPA effort to update its asbestos risk assessment, estimated $K_C = 4 \times 10^{-10}$ and K_A, a potency value for amphibole asbestos (amosite and crocidolite combined), to be 3×10^{-8}. The potency gradient for these values is 1:750 for chrysotile versus amphibole asbestos. The Berman and Crump potency gradient is not directly comparable to the Hodgson and Darnton gradient because the two studies used different measures of exposure. The studies analyzed by Hodgson and Darnton reported exposures based on light microscopy measurements of fibers longer than 5 μm, wider than 0.25 μm, and aspect ratio (length to width) of 5:1. Berman and Crump relied on the same historical occupational studies, but restated the exposure data to reflect only asbestos fibers longer than 10 μm, diameters at most 0.40 μm, and aspect ratio 5:1.

The parameter, k, the exponent for TSFE, has been studied for many types of cancer.[10,11] In general, cancer risk increases with age or TSFE raised to a power between 2.0 and 6.0.[10] Cook, Doll, and Fellingham[10] suggest that k might be a biological constant characteristic of the tissue in which the cancer is produced. For mesothelioma, values of k between 2.5 and 4.0 have been estimated from occupational exposure and risk data in the same studies that have been used to estimate the potency parameters. The value of k most often used in applications of the mesothelioma risk model is 3.0.[4–7,9,13]

2.3. Exposure Variables and Exposure Profile

The exposure variables are: age at diagnosis of mesothelioma, ages at initial and final dates of each discrete exposure, the average intensity of each discrete exposure in f/cc units, and the fiber type for each discrete exposure. An exposure profile is a time sequence description of exposure to asbestos. Exposure profiles typically are estimated using exposure reconstruction methods.[14] For a particular individual, the exposure data may be obtained through interviews with the individual, family members, employers, co-workers, and from employment records. Asbestos fiber type may be determined from job descriptions, product descriptions, and product names. Work history records may contain data on intensity, but if not, intensity data may be estimated from the industrial hygiene and epidemiology literature or government publications that describe studies where occupational measurements obtained during actual or simulated work activities involving asbestos-containing materials (ACM) are reported. The description of an individual's work activities can be matched to these studies to estimate exposure intensities.

2.4. Apportionment Example: Exposure

We explain the apportionment method further with an example. Using a hypothetical worker, we have constructed an exposure profile that demonstrates the essential characteristics of the apportionment method.

Consider a male who began working as a home repair/remodeling handyman in 1955 at the age of 20 years. His activities were a mix of the following: wall demolition and reconstruction; floor replacement, repair; replacement of plumbing fixtures and pipes; and roofing repairs. He continued in this job for 20 years. The materials he worked with contained only chrysotile asbestos. In 1975 at the age of 40 years he concluded his career in home repair/remodeling work and began work as a general laborer in a manufacturing plant where his principal responsibility was assisting with maintenance, repair, and replacement of pipe and boiler systems. The pipe and boiler insulation contained both chrysotile and amosite asbestos. He remained in this job until retirement in 1990 at the age of 55 years. In 2003, at the age of 68 years, he was diagnosed with mesothelioma.

The exposure profile for this individual is summarized in Table I. The table displays a row for each specific discrete exposure and a summary row for each set of similar exposures. For this example, we use values for *Average Exposure Intensity* from the regulatory literature. The exposure intensities for pipe and boiler work in Table I are the OSHA permissible exposure limits (PELs) that were in force during the years in question. The exposure intensity for home repair and remodeling is based on an upper bound average calculated from OSHA's analysis of exposure to support its PEL revision in 1994.[15]

Table I. Hypothetical Asbestos Exposure Profile

Exposure Source	Activity	Asbestos Fiber Type	Start Age	End Age	Duration (Yrs)	Average Exposure Intensity (f/cc)	Hours per Day	Days per Year	Annual Average 8-Hr Daily Exposure (f/cc)	Cumulative Lifetime Exposure (f-yrs/cc)
Plaster, wallboard, joint compound, flooring, plumbing materials, roofing materials	Home repair and remodeling	Chrysotile	20	40	20	0.85	8	240	0.85	17.0
Pipe and boiler insulation	Maintenance, repair, replacement	Chrysotile and amosite (50%/50%)	40	41	1	5.0	8	240	5.0	5.0
			41	51	10	2.0	8	240	2.0	20.0
			51	55	4	0.2	8	240	0.2	0.8
SUMMARY: Pipe and boiler insulation	Maintenance, repair, replacement	Chrysotile and amosite (50%/50%)	40	55	15	1.72	8	240	1.72	25.8

Note: Male; born 1935; diagnosed with mesothelioma at age 68 years.

Annual Average Eight-Hour Daily Exposure is the exposure intensity estimate that is equivalent to an eight-hour per day occupational exposure for 240 days per year. This adjustment is necessary because the mesothelioma potency parameters apply to occupational exposures. The adjustment factor is the product of the following ratios: exposure hours per day divided by 8; and days per year divided by 240.

The rightmost column of Table I displays the contribution to *Cumulative Lifetime Exposure* for each specific discrete exposure. *Cumulative Lifetime Exposure* is calculated as *Duration* of exposure in years multiplied by *Annual Average Eight-Hour Daily Exposure*. *Cumulative Lifetime Exposure* is not the exposure measure that is used in the mesothelioma risk model, but it is an informative exposure index that, in general, is correlated with risk of asbestos-related diseases and is suggestive of the apportionment of risk among exposure sources.

2.5. Apportionment Example: Risk

Table II displays risk estimates for the exposure profile in Table I. Each asbestos exposure in Table I contributes to mesothelioma risk according to the formula $K_i \cdot f_i \cdot ([T - t_{Fi} - 10]^k - [T - t_{Li} - 10]^k)$, where $k = 3.0$, $T = 68$, and $\{f_i\}$, $\{t_{Fi}\}$, and $\{t_{Li}\}$ are *Annual Average Eight-Hour Daily Exposure, Exposure*

Table II. Risk Apportionment Results for Exposure Profile in Table I

Exposure Source	Activity	Start Age	End Age	Asbestos Fiber Type	Annual Average 8- Hour Daily Exposure (f/cc)	Risk Percent (%)
Plaster, wallboard, joint compound, flooring, plumbing materials, roofing materials	Home repair and remodeling	20	40	Chrysotile	0.85	2.3
SUMMARY: Pipe and boiler insulation	Maintenance, repair, replacement	40	55	Chrysotile and amosite (50%/50%)	1.72	97.7

Note: Male; born 1935; diagnosed with mesothelioma at age 68 years.

Start Age, and *Exposure End Age*, respectively. For apportionment, we need only the ratios of the potency parameters, $\{K_i\}$, not their actual values. Therefore, without loss of generality, $K_C = 1$. Applying the Hodgson and Darnton potency ratio results, we set $K_{Am} = 100$ and $K_{C\&Am} = 50.5$, representing a 50%/50% mix of chrysotile and amosite for exposures associated with maintenance, repair, and replacement of pipe and boiler systems. The risk apportionment for the home repair/remodeling exposure source is 2.3%; for maintenance, repair, and replacement of pipe and boiler systems, the percentage is 97.7%.

3. DISCUSSION

We have described a model (Equation (2)) and a method for apportioning mesothelioma risk among sources of asbestos exposure assumed to contribute to the cause of mesothelioma for an individual. Morgan[(16)] employed a simpler model to calculate contributions to risk from each of a number of specific asbestos exposure sources and interpreted the risk contributions as probabilities of causation. Egilman *et al.*[(17)] criticized Morgan's approach and his interpretation because he assumed that each individual's mesothelioma had exactly one cause occurring in one specific year, did not explicitly differentiate population risk from individual risk, did not differentiate potency among fiber types, and did not address the biological justification for the model. Egilman *et al.* argued, among other things, that Morgan's approach could not be used to estimate causal probabilities for an individual mesothelioma case. The approach we have described addresses the issues raised by Egilman. We do not attempt to identify a particular asbestos exposure among many as the single cause of mesothelioma. Instead, the results are percentages used to apportion mesothelioma risk among multiple contributing asbestos exposure sources.

The method we present is intended for application to individual mesothelioma cases. Although it is not possible at this time to describe the detailed biological mechanism of mesothelioma formation for any specific individual, the risk model for mesothelioma we employed is a reasonable approximation. The mesothelioma model is based on the multistage model for carcinogenesis, which describes the biological process of tumor growth in individuals that eventually leads to malignancy.[(3,5,8)] The parameters in the mesothelioma risk model were estimated from population data. Therefore, the resulting set of percentages used to apportion risk among exposure sources is not unique for an individual, but represents a group of individuals. The group consists of all mesothelioma cases diagnosed at the same age and having the same exposure profile. Allocation percentages derived for the group are applied to every individual member of the group.[2]

For the individual mesothelioma case analyzed in Tables I and II, the group consists of all mesothelioma cases with the exposure profile shown in Table I. To justify application of the group percentages to the individual case, we need to assume that the potency ratios and the exponent of TSFE for the individual are the same as those for the group. If information were available about the individual suggesting a different sensitivity to asbestos fiber types or TSFE, that information could be used to "personalize" the risk equation. To our knowledge, no approaches for personalizing mesothelioma risk have been proposed or evaluated. However, the mesothelioma risk model we employ has as its origin the multistage model for carcinogenesis, which describes the biological process of tumor growth for individuals. Furthermore, the variety of cohort data sets that have been analyzed to estimate potency ratios make it unlikely that personalized model parameter values would differ substantially from those for the group model.

Whatever degree of uncertainty may exist in the apportionment percentages for an individual due to uncertainty in values used for the model parameters may be investigated through sensitivity analysis. Uncertainty in the exposure profile also can be addressed through sensitivity analysis. We suggest that the value assigned to k in sensitivity analyses should be an integer to maintain consistency with its interpretation in the multistage model, which is a building block of the mesothelioma risk model. Current research on mesothelioma risk as well as regulatory applications of the mesothelioma risk model use a value of k equal to 3.0.[(4–7,9,13)] For ratios of the potency parameters, the recent analysis of occupational cohort studies by Hodgson and Darnton indicates a gradient of 1:100:500 for chrysotile, amosite, and crocidolite, respectively.[(12)] Similar research conducted for EPA by Berman and Crump[(9)] indicates a gradient of 1:750 for chrysotile versus amphibole asbestos, although, as explained above, this ratio is not comparable to the Hodgson and Darnton gradient because different

[2] Lagakos and Mosteller[(18)] present justification, in general, for application of group risk to individual cases for apportioning compensation in "Assigned Shares in Compensation for Radiation-Related Cancers."

exposure measures were used. Other estimates of the potency values that would lead to alternative ratios are discussed in Berman and Crump[9] and in EPA's asbestos health assessment update.[6] Exposure estimates typically would be stated with a range of values to characterize uncertainty. We expect uncertainty in the timing variables (i.e., exposure start and end ages) to be relatively small. Exposure intensities usually would be estimated from industrial hygiene measurements, either collected at the point of exposure or reported in industrial hygiene and epidemiological studies. Variation in these estimates may be used to define ranges of uncertainty for use in sensitivity analyses.

4. CONCLUSIONS

Mesothelioma risk is directly related to intensity of exposure, time since exposure began, duration of exposure, and fiber type exposure. Each variable individually provides information for apportioning mesothelioma risk among exposure sources. The mesothelioma risk model in Equation (2) combines these variables to produce a single estimate of the percentage contribution to risk for each specific exposure source. Where compensation has been awarded to an individual, the percentages define an apportionment of that compensation among responsible parties. For occupational disease compensation boards, juries, parties responsible for paying damages, and currently by the U.S. Senate in its efforts to formulate a bill establishing an asbestos settlement trust,[19] the mesothelioma risk model provides a scientifically based, practical, and effective method for apportionment where previously there was none.

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